In the Title

Please amend the title to --ANTI-TNF ANTIBODIES AND METHOTREXATE IN THE TREATMENT OF ARTHRITIS AND CROHN'S DISEASE--.

In the Claims

Please amend Claims 1, 5, 6, 10, 13, 14, 18, 21, 22, 26, 27 and 31 and add Claims 32-37 as follows:

D1

1. (Twice Amended) A method of treating arthritis [an autoimmune or inflammatory disease] in an individual in need thereof comprising co-administering methotrexate and an anti-tumor necrosis factor alpha antibody or an antigen-binding fragment thereof to the individual, in therapeutically effective amounts.

D2

2 ~~5~~. (Three Times Amended) A method of Claim 1 wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is administered in a series of doses separated by intervals of days or weeks.

D3

3 ~~6~~. (Twice Amended) A method of Claim 1 [5] wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for tumor necrosis factor alpha or an antigen-binding portion thereof and a human constant region.

D4

8 ~~10~~. (Twice Amended) A method of treating rheumatoid arthritis in an individual in need thereof comprising co-administering methotrexate and an anti-tumor necrosis factor alpha antibody or an antigen-binding fragment thereof to the individual, in therapeutically effective amounts.

D5

9 ~~13~~. (Twice Amended) A method of Claim ~~10~~ 8 wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is administered in [multiple] a series of doses separated by intervals of days or weeks.

10 8
14. (Twice Amended) A method of Claim ~~10~~ [13] wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for tumor necrosis factor alpha or an antigen-binding portion thereof and a human constant region.

D5 certd

15 18. (Twice Amended) A method of treating Crohn's disease in an individual in need thereof comprising co-administering methotrexate and an anti-tumor necrosis factor alpha antibody or an antigen-binding fragment thereof to the individual, in therapeutically effective amounts.

D6

16 15
21. (Twice Amended) A method of Claim ~~18~~ wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is administered in [multiple] a series of doses separated by intervals of days or weeks.

D7

17 15
22. (Twice Amended) A method of Claim ~~18~~ [21] wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for tumor necrosis factor alpha or an antigen-binding portion thereof and a human constant region.

22
26. (Twice Amended) A composition comprising methotrexate and an anti-tumor necrosis factor alpha antibody or an antigen-binding fragment thereof.

D8

23 22
27. (Twice Amended) A composition of Claim ~~26~~ wherein the anti-tumor necrosis factor alpha antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for tumor necrosis factor alpha or an antigen-binding portion thereof and a human constant region.

28
31. (Three Times Amended) A method of treating arthritis [an autoimmune or inflammatory disease] in an individual in need thereof comprising co-administering to the individual, in

D9

therapeutically effective amounts, methotrexate and a soluble TNFα receptor or functional portion thereof, wherein said soluble TNFα receptor is selected from the group consisting of p55 TNFα receptor and p75 TNFα receptor [an agent which interferes with TNFα, TNFα receptor signalling or TNFα synthesis, in therapeutically effective amounts].

~~32~~ 29. A method of Claim ~~31~~ 28 wherein the soluble TNFα receptor is a TNFα receptor multimeric molecule.

~~33~~ 30. A method of Claim ~~31~~ 28 wherein the soluble TNFα receptor is a TNFα immunoreceptor fusion molecule.

~~34~~ 7. A method of Claim 1 wherein the anti-TNFα antibody or antigen-binding fragment is a humanized anti-TNFα antibody or antigen-binding fragment thereof.

~~35~~ 14. A method of Claim ~~10~~ 8 wherein the anti-TNFα antibody or antigen-binding fragment is a humanized anti-TNFα antibody or antigen-binding fragment thereof.

~~36~~ 21. A method of Claim ~~18~~ 15 wherein the anti-TNFα antibody or antigen-binding fragment is a humanized anti-TNFα antibody or antigen-binding fragment thereof.

~~37~~ 27. A composition of Claim ~~26~~ 22 wherein the anti-TNFα antibody or antigen-binding fragment is a humanized anti-TNFα antibody or antigen-binding fragment thereof.

REMARKS

Applicants' remarks are set forth below with reference to the numbered paragraphs in the Office Action dated November 23, 1999 (Paper No. 20).

Title of the Invention

The title of the invention has been amended to more specifically correspond to the claimed subject matter.